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(54) Title: USE OF BENZIMIDAZOLE ANTHELMINTIC IN THE TREATMENT OF MICROSPORIDIAL INFECTIONS			
(57) Abstract <p>The use of a benzimidazole anthelmintic in the treatment of microsporidial infection.</p>			

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USE OF A BENZIMIDAZOLE ANTHELMINTIC IN THE TREATMENT OF MICROSPORIDIAL INFECTIONS

The present invention relates to the use of certain benzimidazole compounds in the treatment of diseases caused by microsporidia organisms, in particular the treatment of diarrhoea in patients infected with human immunodeficiency virus (HIV).

There are more than 500 species of the protozoa microsporidia which infect animals. Until the advent of acquired immune deficiency syndrome (AIDS) human infection was rare and confined to one or two cases of encephalitis and myositis. Now, however, microsporidium infection is common in the small intestine of HIV infected individuals and is thought to cause diarrhoea. In a recent study in the USA a third of patients in whom no other pathogen as a cause of diarrhoea had been uncovered, were found to have microsporidiosis infection in jejunal biopsy material (Human Pathology, 1990, 21(5), 475-81). Very similar figures were recently obtained in a UK study (Peacock et al., J. Clin. Path. 1991, in press). However, positive proof that Microsporidiosis is of pathogenic importance in the development of diarrhoea requires the ability to eradicate this organism with suitable chemotherapeutic agents or, alternatively, the development of suitable animal models. Such suitable chemotherapeutic agents have, until now, not been available.

The present invention fulfils this need and provides in a first aspect, the benzimidazole anthelmintic albendazole, for use in the manufacture of a medicament for use in the treatment of microsporidia infections, in particular in the treatment of microsporidia infection, for example diarrhoea-causing microsporidial infection, in patients infected with the human immunodeficiency virus (HIV).

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In a broader aspect, the invention provides a benzimidazole anthelmintic for use in the manufacture of a medicament for use in the treatment of microsporidia infections, in particular in the treatment of microsporidia infection, for example diarrhoea-causing microsporidia infection, in patients infected with the human immunodeficiency virus (HIV).

The term 'benzimidazole anthelmintic' is intended to include any benzimidazole containing agent which is known to act as a broad spectrum anthelmintic. For example, in addition to albendazole, such compounds include fenbendazole, oxibendazole, mebendazole and parbendazole.

In a further aspect the present invention provides a method of treatment of microsporidial infection which comprises administration to a subject in need thereof of an effective amount of a benzimidazole anthelmintic, for example albendazole. In particular the invention provides a method for the treatment of microsporidial infection, for example diarrhoea-causing microsporidial infection, in patients infected with the human immunodeficiency virus (HIV).

When used in the present invention, the active agent is formulated in a standard pharmaceutical composition, for example in a tablet composition.

Suitable doses of active agent will be in the range of from 100 to 5000mg per day, the compound being administered in one or more discrete dosage units, once or twice a day, for as long as is necessary to treat the condition and maintain the patient free of infection. The size, frequency and duration of the dosage regimen will, of course, depend on the severity of the infection.

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RESULTS

A study was carried out on 6 HIV infected individuals with diarrhoea and proven microsporidial infection on 5 jejunal biopsy.

The patients were treated with albendazole (400mg, b.i.d.) and within 1 week, 5 of the 6 had had dramatic symptomatic improvement with complete loss of diarrhoea and 10 arrested weight loss. Subsequently, two patients died of non-diarrhoeal causes and of the remaining 4 who completed one month's treatment, two relapsed.

Jejunal biopsies performed following therapy in five of 15 these patients have shown continuing evidence of Microsporidiosis but an apparent maturation arrest so that frequent meronts are seen but mature spores are not.

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CLAIMS:

1. A benzimidazole anthelmintic for use in the manufacture of a medicament for use in the treatment of 5 microsporidial infection.

2. The use according to claim 1 in which the benzimidazole anthelmintic is albendazole.

10 3. The use according to claim 2 in which the patient treated is also infected with human immunodeficiency virus (HIV).

15 4. The use according to claim 3 in which the microsporidial infection is a diarrhoea-causing infection.

INTERNATIONAL SEARCH REPORT

International Application

PCT/GB 92/00522

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all)⁶According to International Patent Classification (IPC) or to both National Classification and IPC
Int.C1.5 A 61 K 31/415

II. FIELDS SEARCHED

Minimum Documentation Searched⁷

Classification System	Classification Symbols
Int.C1.5	A 61 K

Documentation Searched other than Minimum Documentation
to the Extent that such Documents are Included in the Fields Searched⁸III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹

Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	FR,M, 4761 (CHIMETRON) 20 February 1967, see page 1, left-hand column, lines 1-15 ---	1
P,X	AIDS Care, volume 3, no. 4, 19 December 1991, E.K. Bagdades: "Current treatment of opportunistic infections in HIV diseases", pages 461-466, see page 464 ---	1-4
P,X	STN Information Service, file BIOSIS, abstract number 91:446850, "Treatment of intestinal *microsporidiosis* with albendazole", VII International Conference on Aids: Science Challenging Aids; Florence, IT, June 16-21, 1991, 464P, (vol. 1); 460P, (vol. 2), see the whole article ---	1-4
		-/-

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IV. CERTIFICATION

Date of Actual Completion of the International Search

01-06-1992

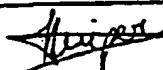
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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		Relevant to Claim No.
Category	Citation of Document, with indication, where appropriate, of the relevant passages	
P,X	J. Protozool, volume 38, no. 6, 1991, Society of Protozoologists, 1991; E.U. Canning et al.: "In vitro and in vivo investigations of human microsporidia", pages 631-635, see page 634	1,2

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.

GB 9200522

SA 57702

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 07/07/92. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-M- 4761		None	